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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,149	11/17/2003	Robert H. Getzenberg	076333-0331	9439

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,149	GETZENBERG, ROBERT H.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment June 6, 2008 in response to the Office Action of March 6, 2008 is acknowledged and has been entered. Claims 1-24 are pending. Claims 2-16 were previously withdrawn. Claims 1 and 17-24 are currently being examined.

Declaration

2. The Declaration of Dr. Robert H. Getzenberg under 37 CFR 1.132 filed June 6, 2008 is sufficient to overcome the rejection of claim 1 under 35 USC 103(a) based upon Kontey et al. (Journal of Urology, March 27, 1997, 157:278 Abstract 1074, IDS) of Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 141-142), and in further view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 1989, p. 18.70-18.75).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 17, 22, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Finlay et al. (J. of Cell Biol. July 1991, 114: 169-183) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 1.

The claims are drawn to:

1. An antibody directed against a nuclear matrix protein or an immunogenic fragment thereof in a human subject, wherein said protein is absent in normal renal cells but

present in cancerous renal cells and is selected from the group consisting of: (a) RCCA-1 having a molecular weight of 53 kD and a pI of 9.30; (b) RCCA-2 having a molecular weight of 32 kD and a pI of 6.95; (c) RCCA-3 having a molecular weight of 27 kD and a pI of 6.50; (d) RCCA-4 having a molecular weight of 20 kD and a pI of 5.25; and (e) RCCA-5 having a molecular weight of 15 kD and a pI of 6.00 or an immunogenic fragment thereof.

17. The isolated antibody of claim 1, wherein the antibody is against RCCA-1 having a molecular weight of 53 kD and a pI of 9.30.

22. The isolated antibody of claim 1, wherein the antibody is a polyclonal antibody.

24. The isolated antibody of claim 1, wherein the antibody is detectably labeled.

Finlay et al. teach a polyclonal antibody to the rat nuclear pore protein p54, which is detectably labeled with ^{125}I protein-A, see page 171-2nd col., 173-1st col. and Figure 2. The nuclear pore protein p54 of Finlay et al. is nucleoporin 54 (Nup54), see Appendix 1.

Cannon et al. teach that RCCA-1 is a differentially spliced form of Nup 54 identified by Ansorge et al., which is CAD97957 see Abstract, p. 1228-2nd col., reference 7, and Appendix 1. An alignment of CAD97957 with the rat Nup 54 shows that the two proteins have two regions of over 100 amino acids with nearly 100 % identity.

Although the reference does not specifically state that the antibodies are directed against RCCA-1, given that the polyclonal antibodies of Finlay et al. bind a polypeptide that has two regions of over 100 amino acids of nearly 100 % identity with RCCA-1, it would be expected that polyclonal antibodies that bind Nup 54 will bind RCCA-1, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order

to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

4. Claims 1, 17, and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Snow et al. (J. Cell Biol. 1 May 1987, 104: 1143-1156) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 1.

The claims are drawn to:

1. An antibody directed against a nuclear matrix protein or an immunogenic fragment thereof in a human subject, wherein said protein is absent in normal renal cells but present in cancerous renal cells and is selected from the group consisting of: (a) RCCA-1 having a molecular weight of 53 kD and a pI of 9.30; (b) RCCA-2 having a molecular weight of 32 kD and a pI of t 6.95; (c) RCCA-3 having a molecular weight of 27 kD and a pI of 6.50; (d) RCCA-4 having a molecular weight of 20 kD and a pI of 5.25; and (e) RCCA-5 having a molecular weight of 15 kD and a pI of 6.00 or an immunogenic fragment thereof.

17. The isolated antibody of claim 1, wherein the antibody is against RCCA-1 having a molecular weight of 53 kD and a pI of 9.30.

22. The isolated antibody of claim 1, wherein the antibody is a polyclonal antibody.

23. The isolated antibody of claim 1, wherein the antibody is a monoclonal antibody.

24. The isolated antibody of claim 1, wherein the antibody is detectably labeled.

Snow et al. teach monoclonal and polyclonal antibodies to the rat nuclear pore protein p54, , which is detectably labeled with ^{125}I protein-A, see Abstract, page 1144-1146., Figs. 1, 2, 4 and 5 and Table 1. The nuclear pore protein p54 of Snow et al. is nucleoporin 54 (Nup54), see Appendix 1.

Cannon et al. teach that RCCA-1 is a differentially spliced form of Nup 54 identified by Ansorge et al., which is CAD97957 see Abstract, p. 1228-2nd col., reference 7, and Appendix 1. An alignment of CAD97957 with the rat Nup54 shows that the two proteins have two regions of over 100 amino acids of nearly 100 % identity.

Although the reference does not specifically state that the antibodies are directed against RCCA-1, given that the polyclonal antibodies of Finlay et al. bind a polypeptide that has two regions of over 100 amino acids of nearly 100 % identity with RCCA-1, it would be expected that not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind RCCA-1, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

5. Claims 1, 18, and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No.: 5,037,744 (Knapp et al. August 6, 1991) as evidenced by Cannon et al. (Urology June 2007, 69: 1227-30) and Appendix 2.

The claims are drawn to:

1. An antibody directed against a nuclear matrix protein or an immunogenic fragment thereof in a human subject, wherein said protein is absent in normal renal cells but present in cancerous renal cells and is selected from the group consisting of: (a) RCCA-1 having a molecular weight of 53 kD and a pI of 9.30; (b) RCCA-2 having a molecular weight of 32 kD and a pI of t 6.95; (c) RCCA-3 having a molecular weight of 27 kD and a pI of 6.50; (d) RCCA-4 having a molecular weight of 20 kD and a pI of 5.25; and (e) RCCA-5 having a molecular weight of 15 kD and a pI of 6.00 or an immunogenic fragment thereof.

18. The isolated antibody of claim 1, wherein the antibody is against RCCA-2 having a molecular weight of 32 kD and a pI of 6.95.

22. The isolated antibody of claim 1, wherein the antibody is a polyclonal antibody.

23. The isolated antibody of claim 1, wherein the antibody is a monoclonal antibody.

24. The isolated antibody of claim 1, wherein the antibody is detectably labeled.

US Patent No.: 5,037,744 teaches polyclonal and monoclonal antibodies to human serum albumin and detectably labeling the antibodies see col. 3-lines 49-62, col. 1-lines 27-35, and cols. 14-15.

Cannon et al. (Urology June 2007, 69: 1227-30) teach RCCA-2 was identified as GI: 763431, which is similar to human albumin, see para. bridging p. 1228-1229. Human serum albumin is 99% identical to GI: 763431 over the first 455 amino acids, see appendix 2.

Although the reference does not specifically state that the antibodies are directed against RCCA-2, given that the polyclonal antibodies of US Patent No.: 5,037,744 bind a polypeptide that is 99% identical to GI: 763431/RCCA-2 over the first 455 amino acids, it would be expected

that not only polyclonal antibodies but also a substantial portion of monoclonal antibodies that bind Nup 54 will bind GI: 763431/RCCA-2, thus, the claimed antibodies appear to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the method of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed antibodies are different from that taught by the prior art and to establish patentable differences. See In re Best, 562 F2nd 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1, 18, and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menaya, J. et al. (Accession No AAA64922, GI: 763431, 10 April 1995), in view of Cannon et

al. (Urology June 2007, 69: 1227-30), in view of Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 141-142, previously cited), and in further view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 1989, p. 18.70-18.75, previously cited).

The claims are drawn to:

1. An antibody directed against a nuclear matrix protein or an immunogenic fragment thereof in a human subject, wherein said protein is absent in normal renal cells but present in cancerous renal cells and is selected from the group consisting of: (a) RCCA-1 having a molecular weight of 53 kD and a pI of 9.30; (b) RCCA-2 having a molecular weight of 32 kD and a pI of t 6.95; (c) RCCA-3 having a molecular weight of 27 kD and a pI of 6.50; (d) RCCA-4 having a molecular weight of 20 kD and a pI of 5.25; and (e) RCCA-5 having a molecular weight of 15 kD and a pI of 6.00 or an immunogenic fragment thereof.

18. The isolated antibody of claim 1, wherein the antibody is against RCCA-2 having a molecular weight of 32 kD and a pI of 6.95.

22. The isolated antibody of claim 1, wherein the antibody is a polyclonal antibody.

23. The isolated antibody of claim 1, wherein the antibody is a monoclonal antibody.

24. The isolated antibody of claim 1, wherein the antibody is detectably labeled.

Menaya et al. teach Accession No AAA64922, GI: 763431.

Cannon et al. (Urology June 2007, 69: 1227-30) teach RCCA-2 was identified as GI: 763431, see para. bridging p. 1228-1229.

Harlow and Lane teach that the usefulness of monoclonal antibodies stems from three characteristics- their specificity of binding, their homogeneity, and their ability to be produced in

unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity. Harlow and Lane teach that because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. Harlow and Lane teach that hybridoma cell lines also provide an unlimited supply of antibodies, see p.141.

Harlow and Lane teach that, although in theory monoclonal antibodies can be used for all of the tasks for which polyclonal antibodies are used, polyclonal antibodies are easier to produce and may be better for specific techniques, see p. 142, first para., and Table 6.1.

Sambrook et al. teach detectably labeling antibodies for immunological detection of proteins by western blots, see p. 18.70-18.75.

It would have been *prima facie* obvious to one of ordinary skill in the art to have produced antibodies to GI: 763431because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. App. & Int. 1990).

Additionally, it would have been *prima facie* obvious and one of ordinary skill in the art would have been motivated to make monoclonal antibodies to GI: 763431 because Harlow and Lane teach the advantages of having an unlimited supply of homogeneous antibodies that have a defined specificity. Additionally, one would have been motivated to produce polyclonal antibodies to GI: 763431 because Harlow and Lane teach that polyclonal antibodies are easier to produce than monoclonal antibodies and may be more useful for specific immunological techniques. Given the conventional nature of the production of monoclonal and polyclonal

antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing monoclonal and polyclonal antibodies against GI: 763431.

Further, it would have been prima facie obvious and one would have been motivated to label the antibodies for use in the well known art method of western to detect GI: 763431. using antibodies that are directly or indirectly labeled with a secondary antibody or other reagent, see Sambrook et al. p. 1870-1875.

Thus, one of skill in the art would be motivated with a reasonable expectation of success to make labeled monoclonal or polyclonal antibodies to the proteins GI: 763431.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1 and 17-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of U.S. Patent No. 6,232, 443 in view of

Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 141-142, previously cited), and in further view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 1989, p. 18.70- 18.75, previously cited).

The antibody used in the method of detection claim 14, which binds RCCA-1, 2, 3, 4 or 5 anticipates the antibody claimed in claims 1 and 17-21, directed against RCCA-1, 2, 3, 4 or 5.

Harlow and Lane teach that the usefulness of monoclonal antibodies stems from three characteristics- their specificity of binding, their homogeneity, and their ability to be produced in unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity. Harlow and Lane teach that because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. Harlow and Lane teach that hybridoma cell lines also provide an unlimited supply of antibodies, see p.141.

Harlow and Lane teach that, although in theory monoclonal antibodies can be used for all of the tasks for which polyclonal antibodies are used, polyclonal antibodies are easier to produce and may be better for specific techniques, see p. 142, first para., and Table 6.1.

Sambrook et al. teach detectably labeling antibodies for immunological detection of proteins by western blots, see p. 18.70-18.75.

It would have been prima facie obvious and one of ordinary skill in the art would have been motivated to make monoclonal antibodies to RCCA-1, 2, 3, 4 or 5 of U.S. Patent No. 6,232,443 because Harlow and Lane teach the advantages of having an unlimited supply of homogeneous antibodies that have a defined specificity. Additionally, one would have been motivated to produce polyclonal antibodies to RCCA-1, 2, 3, 4 or 5 of U.S. Patent No. 6,232,

443 because Harlow and Lane teach that polyclonal antibodies are easier to produce than monoclonal antibodies and may be more useful for specific immunological techniques. Given the conventional nature of the production of monoclonal and polyclonal antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing monoclonal and polyclonal antibodies against RCCA-1, 2, 3, 4 or 5 of U.S. Patent No. 6,232, 443.

Further, it would have been prima facie obvious and one would have been motivated to label the antibodies for use in the well known art method of western to detect RCCA-1, 2, 3, 4 or 5 of U.S. Patent No. 6,232, 443. using antibodies that are directly or indirectly labeled with a secondary antibody or other reagent, see Sambrook et al. p. 1870-1875.

8. All other objections and rejections recited in the Office Action of March 6, 2008 are withdrawn.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/

Examiner, Art Unit 1642

/Karen A Canella/

Primary Examiner, Art Unit 1643

/PJR/